REMARKS

Formal Matters

Pending claims: Claims and 7-9, 16-20, 28, 42-43, 45, 47, 48 and 52-59 and new claims 60-62 are pending. Claims 1-6, 10-15, 21-27, 29-41, 44, 46, 49-51 are canceled as non-elected claims. Claims 7, 16, 54, and 55 are amended and new claims 60-62 are added.

Support for the amendments is found throughout the specification. Claims 7, 54, and 55 are amended and new claims 60-62 are addedto recite that the FSH-R of the invention is encoded by a DNA molecule that hybridizes to a portion of SEQ ID NO:5. Support for the amendment is found throughout the specification such as at page 14, line 35 to page 15, line 8; in the Sequence Listing; and in Figs. 6 and 7. Claim 16 is amended to delete the word "either" as a result of Applicants election of a single species (subject to 37 CFR 1.141). No new matter is added by the amendments.

Restriction and Election Requirements

In response to the restriction requirement mailed July 9, 2002, Applicants elected with traverse Group II (claims 7-29, 42-48 and 52-59 in the response submitted August 1, 2002 (Paper No. 9). In response to the species election requirement mailed September 9, 2002, Applicants elected with traverse the species FSH-R, noting that Applicants have the right under 37 CFR 1.141 (providing that ". . . more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application . . . .) to have the claims prosecuted for the non-elected species when allowable subject matter is determined for the elected species.

Non-elected claims 1-6, 10-15, 21-27, 29-41, 44, 46, 49-51 are canceled without prejudice to later prosecution, leaving claims 7-9, 16-20, 28, 42-43, 45, 47, 48, 52-59 pending in the application. New claims 60-62 are added.

Requirement for Amended Title

The Examiner requires a new title alleging that the current title, Glycoprotein Hormone Receptor Molecules, is not descriptive. Applicants respectfully disagree because as noted above,

while Applicants have elected the species FSH-R, Applicants have the right under 37 CFR 1.141 to have the claims prosecuted for additional non-elected species upon allowance of the claims for the elected species. Under the circumstances, Applicants respectfully defer amending the title until such time as the claims are reevaluated under 37 CFR 1.141.

Compliance with 37 CFR § 1.821(d)

Claims 54-55 and the specification are objected to for allegedly failing to comply with 37 CFR § 1.821(d). Applicants have amended the specification and claims 7, 16, 54 and 55 as well as adding new claims 60-62 to recite the appropriate FSH-R-related sequence ID number as provided in the Sequence Listing submitted August 29, 2001. Support for the amendments is found throughout the specification such as, for example, Fig. 7 and the Sequence Listing. No new matter is added by the amendments.

Priority

Applicants' present application claims priority to PCT/US90/02488, filed 5/4/90, which in turn claims priority to US 07/347,683, filed 5/5/989. Applicants respectfully disagree that the earlier filing lacks adequate written description for the claimed species because, as noted above regarding Applicants' right to a reasonable claim breadth under 35 CFT 1.141, the allowable subject matter is not yet agreed upon.

Judicially Created Double Patenting Rejection

Claims 7-9, 16-20, 42, 43, 47, 48, 52-54, 56, 58, and 59 were rejected under the judically created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-18 of US6,261,800. Applicants respectfully defer discussion of this issue until such time as the Examiner agrees that the claims encompass allowable subject matter.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 16-20 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite because, allegedly, it is not clear in claim 16 to what "*either* said hormone receptor molecule"

refers. Claims 17-20 depend from rejected claim 16. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Because Applicants have elected a single species (subject to 37 CFR 1.141), use of the word "either" has been deleted from claim 16. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 7-9, 16-20, 28, 42, 43, 45, 47, 48, 52-54, and 56-59 are rejected under 35 U.S.C. § 112 because, allegedly, the claims are broadly drawn to any DNA encoding any FS, LH/CG or TSH receptor. Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims.

Applicants claim a recombinant DNA molecule that is a FSH-R and that hybridizes under conditions of 42 °C and 20% formamide to a nucleic acid sequence from nucleotide 122 to and including nucleotide 2155 of SEQ ID NO:5. Applicants conceived of the sequence of a hormone receptor molecule that is a FSH-R and further conceived of related molecules capable of hybridizing to its DNA under high stringency conditions as disclosed in the specification at page 14, line 35 to page 15, line 8. As a result, Applicants have provided written description for the claimed invention. Withdrawal of the rejection and allowance of the claims are respectfully requested.

Rejection Under 35 U.S.C. § 102(a) (Sprengel et al.)

Claims 7-9, 16-20, 28, 42, 43, 45, 47, and 52-59 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Sprengel et al., Mol. Endocrinol. 4:525-530 (1990). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

Sprengel et al. was available to the public on May 11, 1990 as evidenced by the enclosed copy of the front cover and table of contents of the journal in which Sprengel e al. was published. The journal was stamped as received on May 11, 1990, a date after Applicants priority date.

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Thus, Applicants' invention was not known or used by others before the priority date because the information was not available to the public before that date (MPEP 2128.02 and 2132). As a result, Sprengel et al. is not prior art under Section 102(a). Withdrawal of the rejection and allowance of the claims are respectfully requested.

Rejection Under 35 U.S.C. § 103(a) (Sprengel et al.)

Claim 48 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sprengel et al. (*supra*). Applicants traverse the rejection as applied and as it might be applied to the currently pending claims.

For the reasons provided above, the Sprengel et al. reference is not prior art to the present application. Withdrawal of the rejection and allowance of the claims are respectfully requested.

SUMMARY

Claims 7-9, 16-20, 28, 42-43, 45, 47-48, 52-59 and new claims 60-62 are pending in the application. Claims 1-6, 10-15, 21-27, 29-41, 44, 46, 49-51 are canceled due to restriction and election of species (subject to 37 CFR 1.141).

Rejections under Sections 112, first and second paragraph, Section 102(a) and Section 103(a) have been overcome by the discussions provided herein. Withdrawal of the rejections and allowance of the claims is respectfully requested.

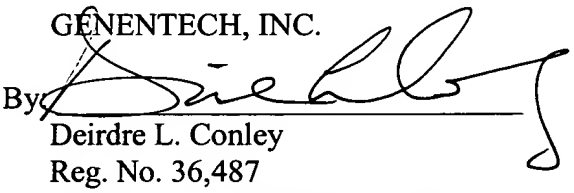
If in the opinion of the Examiner, a **telephone conference** would expedite the prosecution of the subject application, the Examiner is **strongly encouraged** to call the undersigned at the number indicated below.

This response/amendment is submitted with a transmittal letter and petition for a three-month extension of time and fees. In the unlikely event that this document is separated from the transmittal letter, applicants petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Respectfully submitted,

GENENTECH, INC.

Date: May 19, 2003

By: 

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PATENT TRADEMARK OFFICE

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

The specification has been amended as follows, wherein strikeout in brackets [~~00~~] indicates deleted terminology and underling [00] indicates added terminology.

Please replace the paragraph beginning at page 5, line 35, with the following rewritten paragraph:

Figure 6a and 6b show the cDNA [(SEQ ID NO:5)] and predicted amino acid sequence of rat testicular FSH-R [(SEQ ID NO:6 and SEQ ID NO:7)]. Amino acid numbering begins at the N-terminal sequence for the predicted mature receptor protein [(SEQ ID NO:7)], with negative numbers denoting the signal sequence.

Please replace the paragraph beginning at page 5, line 38, with the following rewritten paragraph:

Figure 7 shows structural comparison between the gonadotropin receptors. A) Sequence similarities of receptor domains. The N-terminal half representing the extracellular domain is subdivided into 14 imperfectly duplicated units of approximately 20 residues each and the C-terminal half shows the seven transmembrane segments. Potential glycosylation sites are indicated by filled squares. Different shadings of grey indicate the degrees of sequence conservation for different receptor areas. B) Sequence comparison of receptors in the one letter code. The FSH-R sequence [(SEQ ID NO. 7)] is shown as the lower sequence and differences as well as substitutions in the LH/CG-R [(SEQ ID NO. 3)] are presented above. Dots denote insertions introduced for optimal alignment. The extracellular repeats are numbered and demarked by vertical lines. Conserved cysteine residues in the extracellular domain are denoted by filled ovals. Transmembrane regions TMI-TMVII are boxed. Small arrows indicate conserved cysteine residues in the second and third extracellular loops of the receptor.

Please replace the paragraph beginning at page 53, line 35, with the following rewritten paragraph:

Polyadenylated RNA isolated from rat testicular Sertoli cells was used as a template for reverse transcriptase. The resulting cDNA served for the construction of a library in lgt10. An aliquot (1x106 clones) was screened for clones with sequence similarity to two probes derived from the LH/CG-R cDNA (nucleotides 1-483 and 1499-2604). Several positive clones were isolated and cloned cDNAs sequenced as described in F. Sanger et al., Proc. Natl. Acad. Sci. USA, 74:5463-5467 (1977) after subcloning into M13 vectors (J. Vieira and J. Messing, Meth Enzymol., 153:3-11 (1987)). The nucleotide [(SEQ ID NO:5)] and predicted amino acid sequences [(SEQ ID NO:6 and SEQ ID NO:7)] of this receptor are shown in Figure 6.

Please replace the paragraph beginning at page 54, line 4, with the following rewritten paragraph:

The translation initiation codon at position 1 defines the start of a 2076 nucleotide open reading frame specifying an N-terminal 17 residue signal sequence followed by a largely hydrophilic domain of 348 residues of putatively extracellular location. This domain contains three N-linked glycosylation sites. It is followed by a structure of 264 residues which comprises seven transmembrane segments. These segments are the hallmark of G protein-coupled receptors. Similar to other such receptors, the 63 residue C-terminus of the FSH-R is proposed to be located intracellularly and contains several amino acids (Ser, Thr, Tyr) whose phosphorylation may regulate receptor activity (K. Palczewski et al., Biochemistry, 27:2306-2313 (1988); J.L. Benovic et al., Proc. Natl. Acad. Sci. USA, 83:2797-2801 (1986)). However, these residues are not part of consensus phosphorylation sites as in other receptors. The mature FSH-R [(SEQ ID NO:7] is predicted to comprise 675 amino acids (75K mol. wt.) and to constitute an integral membrane glycoprotein.

Please replace the paragraph beginning at page 54, line 18, with the following rewritten paragraph:

It is illuminating regarding the proposed similarities in function to compare the gonadotropin receptors FSH-R and LH/CG-R [(SEQ ID NOS:7 and 3, respectively)] (Figure 7). Both molecules are of similar size and display the same structural design. On the level of primary structure, the extracellular domains share approximately 50% sequence similarity while the domains defined by the seven transmembrane segments display 80% sequence identity. The areas of highest sequence divergence comprise the N-terminus, a 40 residue region preceding the first transmembrane segment and the 30 residues encompassing the C-terminus.

In the Claims:

Claim 7, 16, 54 and 55 is amended as follows, wherein strikeout in brackets [~~00~~] indicates deleted terminology and underling [00] indicates added terminology.

7. A recombinant DNA molecule having a gene sequence encoding a hormone receptor molecule, wherein said hormone receptor molecule is [~~selected from the group consisting of the LH/CG receptor, the~~] [a] FSH receptor[~~, and the TSH receptor~~][and wherein said DNA molecule is capable of hybridizing at 42°C in 20% formamide to a nucleic acid sequence from nucleotide 122 to and including nucleotide 2155 of SEQ ID NO:5].

16. The recombinant molecule of claim 8 wherein said molecule expresses [~~either~~] said hormone receptor molecule when present in a host cell.

54. The vector of claim[s] 53 wherein said molecule is capable of hybridizing at 42°C in 20% formamide with the DNA sequence [~~encoding the FSH receptor shown in figure 6a and 6b~~][from nucleotide 122 to and including nucleotide 2155 of SEQ ID NO:5].

55. The vector of claim 54 wherein said molecule is the DNA sequence encoding the FSH receptor [~~shown in figure 6a and 6b~~][of SEQ ID NO:6 or SEQ ID NO:7].

New Claims

60. The recombinant DNA molecule of claim 7, wherein said DNA molecule is capable of hybridizing at 50°C in 50% formamide to a nucleic acid sequence from nucleotide 122 to and including nucleotide 2155 of SEQ ID NO:5.

61. A method for producing a hormone receptor which comprises:

(a) constructing a vector that includes a gene sequence which encodes said hormone receptor;

(b) transforming a host cell with said vector comprising the recombinant DNA molecule of claim 60;

(c) culturing said transformed cell in a culture medium under conditions sufficient for said cell to express said gene sequences; and

(d) recovering said expressed hormone receptor; wherein said hormone receptor is a FSH receptor.

62. The vector of claim 53 wherein said molecule is capable of hybridizing at 50°C in 50% formamide with the DNA sequence from nucleotide 122 to and including nucleotide 2155 of SEQ ID NO:5.